Lipofibromatosis-like neural tumor: Case report of a unique infantile presentation

Lipofibromatosis-like neural tumor: Case report of a unique infantile presentation

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A 14-month-old boy presented with a slow-growing, asymptomatic back plaque, which was biopsied and found to have S100 positivity, sparse CD34 staining, and no significant mitotic activity, nuclear pleomorphism, or necrosis; genetic workup found *LMNA-NTRK1* gene fusion, overall consistent with lipofibromatosis-like neural tumor (LPF-NT). LPF-NT is rare, with 14 cases previously reported, and our patient is the first report of this diagnosis in infancy. This case report and literature review includes comparison of similar diagnoses including lipofibromatosis, low-grade malignant peripheral nerve sheath tumor, infantile fibrosarcoma, and dermatofibrosarcoma protuberans and serves to aid detection of LPF-NT presenting in pediatric patients by highlighting similarities and differences that should prompt consideration. LPF-NT shows locally aggressive behavior only and should not be confused with conditions that have potential for distant spread. However, case reports of metastasizing *LMNA-NTRK1* tumors draw into question whether growths with this gene fusion exist on a spectrum of disease severity. Our patient was treated with wide local excision and has developed no complications or evidence of recurrence with 6 months of follow-up time. (J Am Acad Dermatol 2018;4:185-8.)

Key words: infantile mesenchymal tumor; lipofibromatosis-like neural tumor; pediatric skin tumor.

INTRODUCTION

Infantile mesenchymal tumors can range from benign to malignant, and proper diagnosis is crucial for patient management and counseling. Clinical appearance is not sufficient for diagnosis, and histopathology must be performed to determine tumor type. Lipofibromatosis-like neural tumor (LPF-NT) is a recently defined entity that commonly shows infiltrative growth and spindle cells arranged in streaming fascicles, which is similar to lipofibromatosis, but the tumor is distinguished by S100 protein reactivity and *NTRK1* gene rearrangements. Clinically, differential diagnoses other than lipofibromatosis include peripheral nerve sheath tumor, dermatofibrosarcoma protuberans, infantile fibrosarcoma, hamartoma, myofibroma, vascular plaque such as arteriovenous malformation, congenital nevus with proliferative nodules, and melanoma.

Abbreviations used:

LPF:	lipofibromatosis
LPF-NT:	lipofibromatosis-like neural tumor
FISH:	fluorescence in situ hybridization

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Fig 1. Lipofibromatosis-like neural tumor in a 14-month-old child, presenting as a hyperpigmented left lower back plaque.

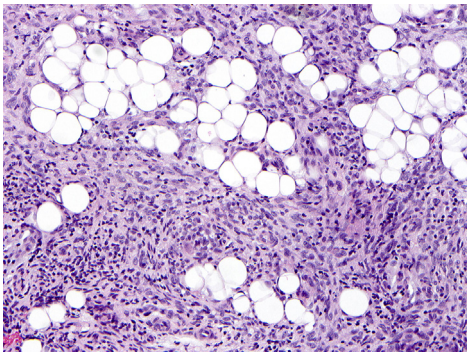

Fig 2. Lipofibromatosis-like neural tumor. Histopathologic sections of the skin biopsy specimen of this patient showed fascicles of spindled tumor cells infiltrating subcutaneous adipose tissue without significant cytomorphologic atypia or mitotic activity. (Hematoxylin-eosin stain; original magnification: ×20.)

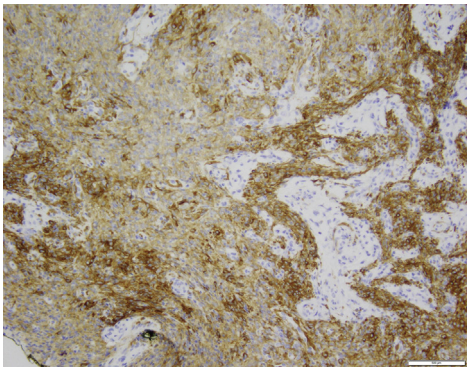

Fig 3. Lipofibromatosis-like neural tumor. NTRK1 immunohistochemistry of this patient's tumor shows positive staining in tumor cells (immunoreactivity indicated by brown chromogen). (Original magnification: ×10.)

REPORT OF A CASE

An otherwise healthy 14-month-old boy presented for evaluation of an asymptomatic truncal "birthmark" that slowly grew and changed color. He was born at 40.5 weeks via cesarean section after an uncomplicated pregnancy. Results of lower back ultrasound scan and radiography performed on the fifth day of life, because of to a small tuft of hair over the lower lumbar spine, were unremarkable. His parents reported the tumor to be present at birth, and his pediatrician documented a quarter-sized plaque at his 2-month visit. At age 9 months, the tumor measured 1.5 × 2 cm with central clearing. The plaque was not pruritic, painful, or friable.

With presentation to the dermatology department at age 14 months, physical examination found a 3- × 3.5-cm violaceous, hyperpigmented, atrophic plaque on his left lower back (Fig 1). It contained 2 prominent erythematous firm nodules, the larger nodule measuring 1.5 cm. Magnetic resonance imaging found a well-defined 3.8- × 3.4- × 0.6-cm discoid mass involving the skin and subcutaneous tissue with predominant T2 hyperintensity, intermediate T1 signal, and a small internal fat signal component.

Histology found a deep dermal and subcutaneous spindled-cell neoplasm with fascicular growth and infiltration into the adipose tissue but no significant mitotic activity, nuclear pleomorphism, necrosis, or hemangiopericytoma-like vascular proliferation (Fig 2). Tumor cells displayed focal S100 protein reactivity and very focal to weak CD34 staining but were negative for desmin, smooth muscle actin, epithelial membrane antigen, and anaplastic lymphoma kinase. Cytoplasmic NTRK1 immunohistochemistry showed diffuse positive staining (Fig 3), and fluorescence in situ hybridization (FISH) studies with custom Bacterial Artificial Chromosomes (BAC) probes found *NTRK1* breakapart. Further fusion FISH assays showed *LMNA-NTRK1* fusion, whereas testing for *ETV6* or *EWSR1* gene rearrangements was negative. Overall findings were most consistent with a diagnosis of LPF-NT.

The tumor was excised with 1-cm margins. The patient had a temporary vacuum-assisted closure to allow for confirmation of clear margins by formalin-fixed and paraffin-embedded pathology evaluation, and the defect was repaired with bilateral V-Y advancement flaps. The patient has no complications or evidence of clinical recurrence with 8 months of follow-up. Three months after excision, magnetic resonance imaging showed no definitive evidence of residual or recurrent tumor; this finding serves as a postoperative imaging baseline.

DISCUSSION

Lipofibromatosis (LPF) tumors, first described in 2000 by Fetsch and colleagues,[1] are rare,

Table I. Key features of LPF-NT and related tumors

	Lipofibromatosis-like neural tumor	Lipofibromatosis	Low-grade malignant peripheral nerve sheath tumor	Infantile fibrosarcoma	Dermatofibrosarcoma protuberans
Atypia	Low	Low	Nuclear atypia present	High	Variable
Mitotic rate	Low	Low	Low	High	Variable
Immunohistochemistry					
S100	Positive	Negative	Positive	Negative	Negative
CD34	Focal to multifocal positivity	Variable	Positive	Negative	Strongly positive
SOX10	Negative	Not reported	Variable	Not reported	Negative
Reported genetic mutations	*NTRK1* rearrangement	Negative for *NTRK1* rearrangement*	*Neurofibromin 1*, *PTEN*, *IGF1R*, *EGFR*, *MAPK*	*ETV6-NTRK3* fusion†	91% with *COL1A1-PDGFB* fusion
Natural history	Local recurrence with incomplete excision	Local recurrence with incomplete excision	Potential for distant metastasis; 50% occur in patients with neurofibromatosis type I	Potential for distant metastasis	Potential for distant metastasis

*One report of balanced translocation (4;9;6).[4]
†One report of *LMNA-NTRK1* fusion.[9]

slow-growing soft tissue masses composed of adipocytic and fibroblastic elements. In reviewing 827 fibromatous tumors from more than 30 years of pathology data, these authors identified 45 cases that they proposed to be classified as LPF. LPF is distinguished from infantile and juvenile fibromatosis by its predominantly adipocytic composition and differentiated from fibrous hamartoma of infancy by its lack of immature mesenchymal tissue. Although LPF tumors are likely to present with ill-defined margins and infiltrative growth, they are distinguished from malignant lesions by their absent-to-rare mitotic figures and mild atypia.[1-7]

In 2016, Agaram and colleagues[8] identified LPF-NT as a related tumor distinguished by S100 protein reactivity, which is indicative of neural differentiation. FISH analysis found that 10 of these 14 initially reported LPF-NT cases contained *NTRK1* gene rearrangements, including *TPR-NTRK1, TPM3-NTRK1,* and most commonly, *LMNA-NTRK1*. In contrast, 25 typical LPF tumors showed S100 protein reactivity or *NTRK1* gene abnormality.

Our case represents the first infantile LPF-NT, as previous patients presented between the ages of 4 and 38 years. This patient had tumor admixture with adipose tissue, which is a key feature of LPF, but relative paucity of fat compared to previously described cases resulted in his tumor appearing fibrous clinically. Identification and report of further LPF-NT cases is required to determine whether this particular presentation is associated with his young age, as infants are known to demonstrate different fat distributions than older patients, as opposed to those characteristic of LPF-NT. Nevertheless, we recommend that LPF-NT be included in the differential diagnosis for patients presenting with masses that are clinically concerning for fibrous as well as fatty tumors. Table I provides an overview of key clinical and histopathologic features that differentiate LPF-NT from related tumors. LPF-NT is associated with locally aggressive behavior only and should not be confused with tumors that distantly metastasize.[8] However, 2 sarcoma cases with the same genetic fusion raise concern for potential disease evolution over time. Agaram and colleagues[8] describe a 37-year-old patient whose tumor was stable for more than 20 years before growing rapidly. Histopathologic and genetic evaluation found S100 positivity, focal CD34 positivity, and *LMNA-NTRK1* gene fusion, features that are characteristic for LPF-NT but not generally found in sarcoma, but the tumor was distinguished as malignant by high mitotic activity and necrosis. Wong and colleagues[9] report a 7-month-old patient with a "purplish lesion on his right buttock" found to have *LMNA-NTRK1* gene fusion and CD34 positivity, without report of S100 protein reactivity. This tumor was diagnosed as infantile fibrosarcoma because of its rapid growth, friability, vimentin positivity, and mitotic figures,

although *LMNA-NTRK1* gene fusion and CD34 positivity are not typical for this diagnosis. Both sarcoma patients went on to have pulmonary metastases, and the younger patient also suffered progression to his S5 vertebral body and acetabulum. Although these tumors were histopathologically distinct from LPF-NT, overlapping genetic features raise concern for the possibility that over time, LPF-NT may accumulate genetic abnormalities and increasingly aggressive clinical characteristics.

This case is reported to increase awareness of LPF-NT, as identification of additional cases will improve understanding of this rare dermatologic condition. Surgical margin guidelines are not available for these tumors, and LPF and LPF-NT have been found to show local recurrence when incompletely excised,[1,8] which prompted our use of 1-cm clinical margins and confirmation of histologic clear margins by formalin-fixed tissue before repair. In the absence of long-term follow-up data, we suggest early diagnosis, complete excision, and close follow-up for those affected.

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